## ABSTRACT

The present invention is based, in part, on expression studies of IL-2 and IL-15 receptor subunits by cycling T cells *in vivo*. In one embodiment, the invention generally features novel combinations of IL-2 and IL-15 antagonists and methods of suppressing the immune response by administering these antagonists. In each case, suppression is achieved by administration of a first agent that targets an IL-15 molecule or an IL-15 receptor (IL-15R) and a second agent that targets an IL-2 molecule or an IL-2 receptor (IL-2R). More generally, the invention features novel combinations of agents that, when administered to a patient (or to a transplant *ex vivo*), reduce the number of antigen-reactive T cells. For example, the invention features compositions (*e.g.*, pharamaceutically acceptable compositions) that include two or more agents, each of which promote T cell death. Alternatively, the composition can contain at least one agent that promotes T cell death and at least one agent that inhibits T cell proliferation. The agent that promotes T cell death can promote AICD (activation induced cell death), passive cell death, ADCC (antibody dependent cell-mediated cytotoxicity) or CDC (complement directed cytotoxicity).